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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,321	12/12/2001	Mitsuru Shiraishi	2614 USOP	2839

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 08/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,321	SHIRAISHI ET AL.	
	Examiner	Art Unit	
	Brenda Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 32-39* is/are pending in the application.

4a) Of the above claim(s) *32-34* is/are withdrawn from consideration.

5)☒ Claim(s) *1,3-23,25 and 37* is/are allowed.

6)☒ Claim(s) *2,24,26,35,36,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-26 and 32-39 are pending in the application.

This action is in response to applicants' amendment filed May 18, 2004. Claims 27-31 were canceled and claims 38 and 39 are newly added.

The applicants requested consideration of the Preliminary Amendment filed December 12, 2001. Since the first Preliminary Amendment included the amendments to claims 1, 4-8, 10, 12-17, 23, 25, 26, 29, 30, 35 and 37 it is herein acknowledged that this amendment has been fully considered in view of the rejections of the claims in the previous office action.

Response to Amendment

Applicant's amendments filed May 18, 2004 have been fully considered with the following effect:

1. The applicants' amendments are sufficient to overcome the objection to the specification labeled paragraph 3 of the last office action, which is hereby **withdrawn.**

2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 2 and 24 of the last office action, applicants' state that "the term is adequately enabled, as support for the term is found in the specification at page 51, lines 19 - page 53, line 5". However, the definition of prodrug in the specification is such that pro-drug refers to "compound which is converted to Compound (I) under the physiological condition or with a reaction due to an enzyme, an gastric acid, etc. in the living body, that is a compound which is converted to Compound (I) with oxidation, reduction, hydrolysis, etc.

according to an enzyme, a compound which is converted to Compound (I) with hydrolysis by gastric acid, etc.; etc.".

The term pro-drug is of indeterminate scope in that they vary widely from drug to drug. It is not known which moiety of formula (I) would form the basis for the pro-drug. Every ester, amide and carbamate in theory is biohydrolyzable, i.e. is capable in some degree of hydrolyses. Not to mention the many in vivo environments that this occurs in. It is the Wands factors, which are used to evaluate the enablement question. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant invention, has claims which embrace substituted benzoazepine compounds. The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would no how to prepare the various compounds suggested by claims 2 and 24. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claims 2 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

3. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 26-31 and 36 of the last office action, applicants' state that claims 27-31 have been cancelled, rendering the aspect of the rejection related to these claims moot and that neither claim 26 or claim 36 contains the term "prevention". However, the 35 U.S.C. § 112, first paragraph rejection of claims 26 and 36 is to the enablement of the compounds for antagonizing the CC chemokine receptor. Recent journal article provided herein, indicates that there are more than 10 different CC chemokine receptors of which the applicants only specifically identify one. The method of antagonizing all CC chemokine receptors as claimed in claim 36 is not remotely enabled. Horuk clearly identifies 10 different CC chemokine receptors of which have varying pathophysiological implications. Horuk also suggests that CCR5 may play a part in patients with rheumatoid arthritis.

Claims 26, 36 and newly added claim 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

4. The applicants' amendments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), b), c), d) and e) of the last office action, which

are hereby **withdrawn**. However, with regards to the 35 U.S.C. § 112, second paragraph rejection labeled f) and g) maintained in the last office action, the applicant's amendments and remarks have been fully considered but they are not persuasive.

f) The applicants' state that "claim 36 is not vague, and request that the Examiner review the support for the claim found on page 74, line 11 – page 76, line 21 iter alia (wherein dosage is discussed)" and that claims which recite methods for antagonizing CCR5 have been found to be patentable by the U.S. Patent and Trademark Office". First, I will not comment on that which was done by others in other applications and/or patents. I am not aware of the facts in those applications and hence am not in a position to comment on what was done by another examiner. I can only comment on the facts of the instant application as set forth below.

Horuk Cytokine and Growth Factor Reviews herein provided is speculative at best with respect to the use of CCR5 for anything other than HIV-1. Horuk also stated that the chemokine receptor CCR5 is being evaluated for potential therapeutic applications with respect rheumatoid arthritis. Thus the treatment of diseases based solely on "antagonizing CCR5 or CC chemokine receptor of which there are many" does not provide for the treatment of every disease and/or disorder claimed herein. Additionally, the scope of diseases and/or disorders associated with chemokine receptors could alter over time. The applicants' are not entitled to preempt the efforts of others. The applicants' are only entitled to

those diseases and/or disorders associated with serotonin receptors at the time of filing.

Claims 36 and newly added claim 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

g) The applicants' state that "the phrase simply indicates that treatment can be made with a combination of: a compound of claim 1 or a salt thereof with a protease inhibitor; a compound of claim 1 or a salt thereof with a reverse transcriptase inhibitor or a compound of claim 1 or a salt thereof with a protease inhibitor and a reverse transcriptase inhibitor". However, it is not known with what protease inhibitor or reverse transcriptase inhibitor.

Claim 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

5. The applicants filing of a terminal disclaimer is sufficient to overcome the obviousness-type double patenting rejection of claims 1, 3-23, 25 and 26 labeled paragraph 7 in the last office action, which is hereby **withdrawn**.

6. The applicants filing of a terminal disclaimer is sufficient to overcome the obviousness-type double patenting rejection of claims 25-31 and 35-37 labeled paragraph 8 in the last office action, which is hereby **withdrawn**.

In view of the amendment dated May 18, 2004, the following new grounds of rejection apply:

Election/Restrictions

7. Claims 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 1, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 35 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reason(s) apply:

a) Claim 35 is vague and indefinite in that it is not known what is meant by infectious diseases of HIV.

b) Claim 35 is vague and indefinite in that it is not known what is meant by infectious disease of HIV.

Allowable Subject Matter

9. Claims 1, 3-23, 25 and 37 are allowed. None or the prior art of record or a search in the pertinent art area teaches the compounds and method of use of the compounds of formula I as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brenda Coleman

Brenda Coleman
Primary Examiner Art Unit 1624
August 1, 2004